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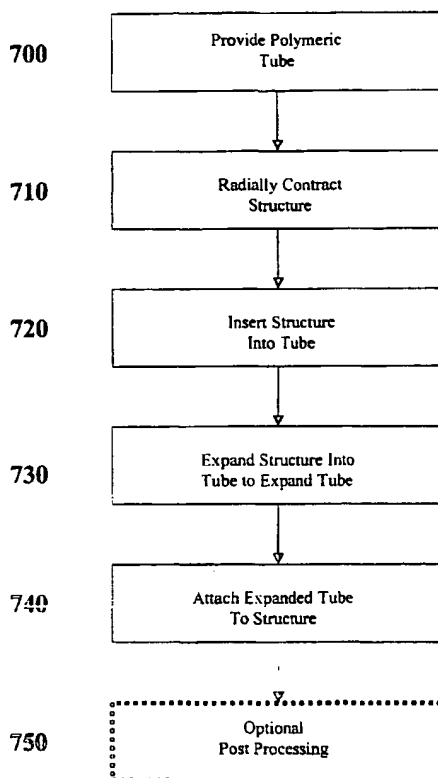
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(54) Title: METHOD OF MAKING A MEDICAL DEVICE HAVING A THIN WALL TUBULAR MEMBRANE OVER A STRUCTURAL FRAME



(57) Abstract: The present invention relates to a medical device and method for making the medical device. In particular, the present invention relates to membrane covered structural frame, and to a method of forming a tubular membrane on a structural frame. In one aspect, a polymeric tube is provided having a first diameter and a first tube wall thickness. A radially expandable and contractible structural frame is radially contracted, and inserted into at least a portion of the structural frame. The radially contracted structural frame then expands to expand the polymeric tube to a second diameter, wherein the second diameter is greater than the first diameter. As the polymeric tube radially expands, the tube wall thickness becomes thinner, so that the polymeric tube becomes a thin walled tubular membrane. The polymeric tube and structural frame are then mechanically attached to each other.

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METHOD OF MAKING A MEDICAL DEVICE  
HAVING A THIN WALL TUBULAR  
MEMBRANE OVER A STRUCTURAL FRAME

5 FIELD OF THE INVENTION

The present invention relates to a medical device and method of making the medical device. In particular, the present invention relates to a medical device having a radially expandable structural frame and a thin wall tubular  
10 membrane structure, and a method of making the medical device having a thin wall tubular membrane on a radially expandable structural frame.

BACKGROUND OF RELATED ART

15 The human body has numerous biological valves that control fluid flow through body lumens and vessels. For example the circulatory system has various heart valves that allow the heart to act as a pump by controlling the flow of blood through the heart chambers veins, and aorta. In  
20 addition, the venous system has numerous venous valves that help control the flow of blood back to the heart, particularly from the lower extremities.

These valves can become incompetent or damaged by disease, for example, phlebitis, injury, or the result of an  
25 inherited malformation. For example, heart valves are

subject to disorders, such as mitral stenosis, mitral regurgitation, aortic stenosis, aortic regurgitation, mitral valve prolapse and tricuspid stenosis. These disorder are potentially life threatening. Similarly, incompetent or  
5 damaged venous valves usually leak, allowing the blood to improperly flow back down through veins away from the heart (regurgitation reflux or retrograde blood flow). Blood can then stagnate in sections of certain veins, and in particular, the veins in the lower extremities. This  
10 stagnation of blood raises blood pressure and dilates the veins and venous valves. The dilation of one vein may in turn disrupt the proper function of other venous valves in a cascading manner, leading to chronic venous insufficiency. In addition, the vessels and body lumens may become damaged  
15 and require repair.

Numerous therapies have been advanced to treat symptoms, including the correction of incompetent valves. Similarly, the vessels and body lumens may become damaged and require repair. Less invasive procedures include  
20 compression, elevation and wound care. However, these treatments tend to be somewhat expensive and are not curative. Other procedures involve surgical intervention to

repair, reconstruct or replace the incompetent or damaged valves, particularly heart valves, and vessels.

Surgical procedures for incompetent or damaged venous valves include valvuloplasty, transplantation, and  
5 transposition of veins. However, these surgical procedures provide somewhat limited results. The leaflets of venous valves are generally thin, and once the valve becomes incompetent or destroyed, any repair provides only marginal relief. Surgical procedures to repair damaged vessels or  
10 body lumens include delivering and implanting expandable grafts and/or replacing damaged vessels.

As an alternative to surgical intervention, drug therapy to correct valvular incompetence has been utilized. Currently, however, there are no effective drug therapies  
15 available.

Other means and methods for treating and/or correcting damaged or incompetent valves and lumens include utilizing xenograft valve transplantation (monocusp bovine pericardium), prosthetic/bioprosthetic heart valves and  
20 vascular grafts, and artificial venous valves. These means have all had somewhat limited results.

What is needed is an artificial endovascular valve for the replacement of incompetent biological human valves,

particularly heart and venous valves. These valves may also find use in artificial hearts and artificial heart assist pumps used in conjunction with heart transplants. What is also needed is an artificial endovascular conduit for the  
5 repair of incompetent or damaged vessels or body lumens.

#### SUMMARY OF THE INVENTION

The present invention relates to a medical device, and in particular, a method of placing a tubular membrane on a  
10 radially expandable structural frame. One example of a medical device having a radially expandable structural frame and a tubular membrane is a stent-based valve. Another example might include medical devices, such as grafts and stent grafts, to repair and/or treat vascular aneurysms,  
15 such as abdominal aortic aneurysms.

One embodiment of the radially expandable structural frame comprises a proximal anchor and a distal anchor. The proximal and distal anchors are formed from a lattice of interconnected elements, and have a substantially  
20 cylindrical configuration with first and second open ends and a longitudinal axis extending there between.

The radially expandable structural frame also comprises one or more struts, each having a first and a second end.

The first end of each strut is attached to the proximal anchor and the second end of each strut is attached to the distal anchor. The tubular membrane assembly is placed on the radially expandable structural frame.

5       The present invention provides a method of placing the tubular membrane about a radially contractible and expandable structural frame. In accordance with one aspect, the method of the present invention comprises the steps of providing a polymeric tube having a first diameter and a  
10 first wall thickness. A structural frame is then radially contracted. The radially contracted structural frame is then placed, at least in part, into the polymeric tube. Once the radially contracted structural frame is placed at the desired location, the structural frame expands into the  
15 polymeric tube, expanding at least a part of the polymeric tube to a second diameter, and forming a covered frame assembly. The second diameter of the polymeric tube is greater than the first diameter. The expanded polymeric tube and structural frame are then mechanically attached.  
20 One method of mechanical attachment includes coating the covered frame assembly with a polymer.

A medical device having a tubular membrane structure and a radially expandable structural frame is also

contemplated by the present invention. The medical device comprises an outer membrane formed at least in part from a polymeric material, preferably a polymeric tube positioned and radially expanded over a radially expandable structural frame, such that the radially expanded polymeric tube form a thin membrane cover over the structural frame. An outer coating formed at least in part from a polymer solution is coated over the radially expanded polymeric tube and structural frame, such that the outer coating mechanically attaches the outer membrane to the radially expandable structural frame.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1A shows a perspective view of a prosthetic venous valve in the deployed state according to one embodiment of the present invention.

Figure 1B shows a perspective view of the prosthetic venous valve structural frame in the deployed state according to one embodiment of the present invention.

Figure 1C shows a perspective view of the prosthetic venous valve structural frame having helical connecting members according to one embodiment of the present invention.



Figure 1D shows a perspective view of the prosthetic venous valve structural frame having an hourglass shape according to one embodiment of the present invention.

Figure 2A shows a perspective view of the proximal  
5 stent-based anchor in the expanded deployed state according to one embodiment of the present invention.

Figure 2B shows a close-up perspective view of a loop having inner and outer radii according to one embodiment of the present invention.

10 Figure 2C shows a perspective view of the prosthetic venous valve structural frame having connecting members connected between the proximal and distal anchors in a peak-to-peak configuration according to one embodiment of the present invention.

15 Figure 2D shows a perspective view of the prosthetic venous valve structural frame having connecting members connected between the distal and proximal anchors in a peak-to-valley configuration according to one embodiment of the present invention.

20 Figure 2E shows a perspective view of the prosthetic venous valve structural frame having connecting members connected between the distal and proximal anchors in a

valley-to-valley configuration according to one embodiment of the present invention.

Figure 2F shows a perspective view of the prosthetic venous valve structural frame having connecting members  
5 connected between the distal and proximal anchors along the strut members according to one embodiment of the present invention.

Figure 3 shows a perspective view of the distal stent anchor having a plurality of hoop structures according to  
10 one embodiment of the present invention.

Figure 4A is a perspective view illustrating one embodiment of the expanded (deployed) prosthetic venous valve assembly in the open position.

Figure 4B is a section view illustrating one embodiment  
15 of the expanded (deployed) prosthetic venous valve assembly in the open position.

Figure 5A is a perspective view illustrating one embodiment of the expanded (deployed) prosthetic venous valve assembly in the closed position.

20 Figure 5B is a section view illustrating one embodiment of the expanded (deployed) prosthetic venous valve assembly in the closed position.

figure 6A is a perspective view illustrating a membrane limiting means according to one embodiment of the present invention.

Figure 6B is a perspective view illustrating a membrane limiting means according to one embodiment of the present invention.

Figure 6C is a perspective view illustrating a membrane limiting means according to one embodiment of the present invention.

Figure 7 is a flow diagram illustrating the steps to electro-statically spin a tubular membrane on a structural frame according to one embodiment of the present invention.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The stent-based valves disclosed with the present invention provide a method for overcoming the difficulties associated with the treatment of valve insufficiency. Although stent based venous valves are disclosed to illustrate one embodiment of the present invention, one of ordinary skill in the art would understand that the disclosed invention can be equally applied to other locations and lumens in the body, such as, for example, coronary, vascular, non-vascular and peripheral vessels,

ducts, and the like, including but not limited to cardiac valves, venous valves, valves in the esophagus and at the stomach, valves in the ureter and/or the vesica, valves in the biliary passages, valves in the lymphatic system and  
5 valves in the intestines. In addition, the method of placing a membrane assembly over a structural frame can be equally applied to various medical devices having a radially expandable/compressible structural frame, including for example, grafts, stent grafts, and other aneurysm and vessel  
10 repair devices.

In accordance with one aspect of the present invention, the prosthetic valve is designed to be percutaneously delivered through a body lumen to a target site by a delivery catheter. The target site may be, for  
15 example, a location in the venous system adjacent to an insufficient venous valve. Once deployed the prosthetic venous valve functions to assist or replace the incompetent or damaged natural valve by allowing normal blood flow (antegrade blood flow) and preventing or reducing backflow  
20 (retrograde blood flow).

A perspective view of an exemplary prosthetic venous valve in the expanded (deployed) state according to one embodiment of the present invention is shown in Figure 1A.

The prosthetic venous valve 100 comprises a structural frame 101 and a biocompatible membrane assembly 102. In one embodiment, the membrane assembly 102 is comprised of a tubular membrane, valve flaps and valve cusps. The flaps and cusps may be independent components attached to the tubular membrane to form the membrane assembly 102, but are preferably part of, and integrated into, the tubular membrane. In a preferred embodiment, the valve flaps and valve cusps are formed into the tubular membrane by processing techniques as will be discussed in greater detail below.

For clarity, a perspective view of the prosthetic venous valve 100 structural frame 101 is shown in Figure 1B. The structural frame 101 consists of proximal and distal anchor structures 103, 104 connected by at least one connecting member 105. In a preferred embodiment, at least three connecting members 105 are utilized.

It should be noted that the terms proximal and distal are typically used to connote a direction or position relative to a human body. For example, the proximal end of a bone may be used to reference the end of the bone that is closer to the center of the body. Conversely, the term distal can be used to refer to the end of the bone farthest

from the body. In the vasculature, proximal and distal are sometimes used to refer to the flow of blood to the heart, or away from the heart, respectively. Since the prosthetic valves described in this invention can be used in many  
5 different body lumens, including both the arterial and venous system, the use of the terms proximal and distal in this application are used to describe relative position in relation to the direction of fluid flow. For example, the use of the term proximal anchor in the present application  
10 describes the upstream anchor of structural frame 101 regardless of its orientation relative to the body. Conversely, the use of the term distal is used to describe the down stream anchor on structural frame 101 regardless of its orientation relative to the body. Similarly, the use of  
15 the terms proximal and distal to connote a direction describe upstream (retrograde) or downstream (antegrade) respectively.

The connecting members 105 are attached between the proximal and distal anchors 103, 104 to further support the  
20 biocompatible membrane assembly 102 (not shown in Figure 1B). In one embodiment, the connecting members 105 are substantially straight members, connecting the stent based proximal and distal anchors 103, 104 in a direction

substantially parallel to the longitudinal axis 106. Although three connecting members 105 are shown in the illustrated embodiment, this configuration should not be construed to limit the scope of the invention.

5        Alternatively, the connecting members 105 may be twisted in a helical fashion as they extend from the proximal to distal anchors 103, 104. This alternate embodiment is illustrated in Figure 1C. Specifically, the connection points between the connecting members 105 and the  
10        distal anchor 104, and the connecting members 105 and the proximal anchor 103, are rotationally phased 180 degrees from each other to provide the helical design.

Each connecting member 105 may also be biased inward slightly toward the longitudinal centerline 106 of the  
15        stent-based anchors 103, 104, creating a structural frame 101 having an hour-glass shape with the minimum radius located substantially at the longitudinal midpoint along the connecting member 105 length. An hourglass shaped structural frame 101 is illustrated in Figure 1D.

20        The materials for the structural frame 101 should exhibit excellent corrosion resistance and biocompatibility. In addition, the material comprising the structural frame

101 should be sufficiently radiopaque and create minimal artifacts during MRI.

The present invention contemplates deployment of the prosthetic venous valve 100 by both assisted (mechanical) expansion, i.e. balloon expansion, and self-expansion means. In embodiments where the prosthetic venous valve 100 is deployed by mechanical (balloon) expansion, the structural frames 101 is made from materials that can be plastically deformed through the expansion of a mechanical assist device, such as by the inflation of a catheter based balloon. When the balloon is deflated, the frame 101 remains substantially in the expanded shape. Accordingly, the ideal material has a low yield stress (to make the frame 101 deformable at manageable balloon pressures), high elastic modulus (for minimal recoil), and is work hardened through expansion for high strength. The most widely used material for balloon expandable structures 101 is stainless steel, particularly 316L stainless steel. This material is particularly corrosion resistant with a low carbon content and additions of molybdenum and niobium. Fully annealed, stainless steel is easily deformable.

Alternative materials for mechanically expandable structural frames 101 that maintain similar characteristics



to stainless steel include tantalum, platinum alloys, niobium alloys, and cobalt alloys. In addition other materials, such as polymers and bioabsorbable polymers may be used for the structural frames 101.

5       Where the prosthetic venous valve 100 is self-expanding, the materials comprising the structural frame 101 should exhibit large elastic strains. A suitable material possessing this characteristic is Nitinol, a Nickel-Titanium alloy that can recover elastic deformations of up to 10  
10 percent. This unusually large elastic range is commonly known as superelasticity.

The disclosure of various materials comprising the structural frame should not be construed as limiting the scope of the invention. One of ordinary skill in the art  
15 would understand that other material possessing similar characteristics may also be used in the construction of the prosthetic venous valve 100. For example, bioabsorbable polymers, such as polydioxanone may also be used. Bioabsorbable materials absorb into the body after a period  
20 of time, leaving only the biocompatible membrane 102 in place. The period of time for the structural frame 101 to absorb may vary, but is typically sufficient to allow

adequate tissue growth at the implant location to adhere to and anchor the biocompatible membrane 102.

The structural frame 101 may be fabricated using several different methods. Typically, the structural frame  
5 101 is constructed from sheet, wire (round or flat) or tubing, but the method of fabrication generally depends on the raw material form used.

The structural frame 101 can be formed from wire using convention wire forming techniques, such as coiling,  
10 braiding, or knitting. By welding the wire at specific locations a closed-cell structure may be created. This allows for continuous production, i.e. the components of the structural frame 101, such as proximal and distal anchors 103, 104, may be cut to length from a long wire mesh tube.  
15 The connecting member 105 may then be attached to the proximal and distal anchors 103, 104 by welding or other suitable connecting means.

In addition, the complete frame structure may be cut from a solid tube or sheet of material, and thus the  
20 structural frame 101 would be considered a monolithic unit. Laser cutting, water-jet cutting and photochemical etching are all methods that can be employed to form the structural frame 101 from sheet and tube stock.

As discussed above, the disclosure of various methods for constructing the structural frame 101 should not be construed as limiting the scope of the invention. One of ordinary skill in the art would understand that other  
5 construction methods may be employed to form the structural frame 101 of the prosthetic venous valve 100.

In one embodiment of the invention, the anchors 103, 104 are stent-based structures. This configuration facilitates the percutaneous delivery of the prosthetic  
10 venous valve 100 through the vascular system in a compressed state. Once properly located, the stent-based venous valve 100 may be deployed to the expanded state.

A perspective views of a typical stent-based anchor in the expanded (deployed) state is shown in Figures 2A.  
15 Although a Z or S shaped pattern stent anchor is shown for the purpose of example, the illustration is not to be construed as limiting the scope of the invention. One of ordinary skill in the art would understand that other stent geometries may be used.

20 The stent anchors (proximal and distal anchors 103, 104 respectively) each comprise a tubular configuration of structural elements having proximal and distal open ends and defining a longitudinal axis 106 extending there between.

The stent anchors 103, 104 have a first diameter (not shown) for insertion into a patient and navigation through the vessels, and a second diameter D2 for deployment into the target area of a vessel, with the second diameter being  
5 greater than the first diameter. The stent anchors 103, 104, and thus the stent based venous valve 100, may be either a mechanical (balloon) or self-expanding stent based structure.

Each stent anchor 103, 104 comprises at least one hoop  
10 structure 206 extending between the proximal and distal ends. The hoop structure 206 includes a plurality of longitudinally arranged strut members 208 and a plurality of loop members 210 connecting adjacent struts 208. Adjacent struts 208 are connected at opposite ends in a substantially  
15 S or Z shaped pattern so as to form a plurality of cells. As previously discussed, one of ordinary skill in the art would recognize that the pattern shaped by the struts is not a limiting factor, and other shaped patterns may be used. The plurality of loops 210 have a substantially semi-  
20 circular configuration, having an inner radii 212 and outer radii 214, and are substantially symmetric about their centers. The inner and outer radii 212, 214 respectively,

are shown in a close-up perspective view illustrated in Figure 2B.

The connecting member 105 may be connected to the proximal and distal anchors 103, 104 at various points along the structure. As illustrated in Figure 2C, the connecting members 105 are connected between the proximal end of the distal anchor 104 and the distal end of the proximal anchor 103 at the inflection point of the loop members 210. This configuration creates a "Peak-to-Peak" connection bridging the outer radii 214 of the inflection point of loop members 210 on the proximal anchor 103 with the outer radii 214 of the inflection point of the loop member 210 on the distal anchor 104.

Preferably the connecting members 105 are connected to the inflection point of loop members 210 oriented directly opposite one another, and are evenly spaced along the circumference of the tubular anchors 103, 104. This configuration facilitates the radial expansion of the prosthetic valve from the collapsed (delivered) state to the expanded (deployed) state, and provides a substantially symmetrical valve configuration.

Alternatively, the connecting members 105 may be connected between the distal and proximal anchors 104, 103

to create a "Peak-to-Valley" connection between the loop members 210. In this configuration, illustrated in Figure 2D, the connecting members 105 are connected to the proximal end of the distal anchor 104 at the outer radii 214 of the inflection point of loop member 210, and the inner radii 212 of the inflection point of loop member 210 on the proximal end of the proximal anchor 103.

In a further embodiment, the connecting members 105 may be connected between the distal end of the distal anchor 104 and the proximal end of the proximal anchor 103 at the inflection point of the loop members 210 as shown in Figure 2E. This configuration creates a "Valley-to-Valley" connection bridging the inner radii 212 of the inflection point of loop members 210 on the proximal anchor 103 with the inner radii 212 of the inflection point of the loop member 210 on the distal anchor 104.

In still a further embodiment, the connecting members 105 may be connected between the strut members 208 of the distal anchor 104, and the strut members 208 of the proximal anchor 103 as shown in Figure 2F.

In any of the above described configurations, the connections between the connecting members 105 and the anchors 103, 104 may be made at every inflection point

around the circumference of the structure; or alternatively, at a subset of the inflection points around the circumference of the structure. In other words, connected inflection points alternate with unconnected inflection  
5 points in some defined pattern.

Although stent anchors 103, 104 incorporating a singular hoop structure are shown in the embodiment illustrated in Figures 2A through 2F, each stent anchor may utilize a plurality of hoop structures.

10 Figures 3 shows a distal anchor having a plurality of hoop structures 306A through 306D according to another embodiment of the present invention. In the illustrated embodiment, the distal stent anchor 104 may further comprise a plurality of bridge members 314 that connect adjacent  
15 hoops 306A through 306D. Each bridge member 314 comprises two ends 316A, 316B. One end 316A, 316B of each bridge 314 is attached to one loop on one hoop. Using hoop sections 306C and 306D for example, each bridge member 314 is connected at end 316A to loop 310 on hoop section 306C at a  
20 point 320. Similarly, the opposite end 316B of each bridge member 314 is connected to loop 310 on hoop sections 306D at a point 321.

The proximal and distal anchors 103, 104 secure the prosthetic valve 100 to the inside wall of a body vessel such as a vein, and provide anchor points for the connecting members 105. Once deployed in the desired location, the anchors 103, 104 will expand to an outside diameter slightly larger than the inside diameter of the native vessel (not shown) and remain substantially rigid in place, anchoring the valve assembly to the vessel. The connecting members 105 preferably have an inferior radial stiffness, and will conform much more closely to the native diameter of the vessel, facilitating the operation of the biocompatible membrane assembly 102.

The membrane assembly is formed from a flexible membrane-like biocompatible material that is affixed to the frame structure 101. The membrane must be strong enough to resist tearing under normal use, yet thin enough to provide the necessary flexibility that allows the biocompatible membrane assembly 102 to open and close satisfactorily.

Figure 4A and 4B are perspective and section views, respectively, illustrating one embodiment of the expanded (deployed) prosthetic venous valve assembly 100 in the open position. The membrane material may be a biological material, such as a vein or small intestine submucosa (SIS),



but is preferably a synthetic material such as a polymer, for example a micro-cellular foam or porous polymeric material, including expanded Polytetrafluoroethylene (ePTFE), or a bioabsorbable material, such as a  
5 bioabsorbable polymer or bioabsorbable elastomer. Bioabsorbable materials may allow cells to grow and form a tissue membrane (or valve flaps) over the bioabsorbable membrane. The bioabsorbable membrane then absorbs into the body, leaving the tissue membrane and/or flaps in place to  
10 act as a new natural tissue valve.

To achieve the necessary flexibility and strength of the membrane assembly 102, the synthetic material may be reinforced with a fiber, such as an electro-statically spun (ESS) fiber, porous foam, such as ePTFE, or mesh. The  
15 flexible membrane like biocompatible material is formed into a tube (membrane tubular structure 400) and placed over and around the structural frame 101. The membrane tubular structure 400 has a first (distal) and second (proximal) ends 401, 402 respectively, and preferably also has  
20 integrated valve flaps 403 and valve cusps 404. These components together comprise the membrane assembly 102.

The first end 401 of the membrane tubular structure 400 is located between the proximal and distal anchors 103,

104, and is preferably located at the approximate longitudinal midpoint of the connecting members 105 between the two anchors 103, 104. The second end 402 of the membrane tubular structure 400 extends proximally from the  
5 longitudinal midpoint, and is preferably located proximal to at least one half of the proximal anchor 103. In one embodiment of the invention, the membrane structure 400 completely covers the proximal anchor 103. This configuration allows the proximal anchor 103 to expand the  
10 membrane tubular structure 400 into the native vessel wall, anchoring the membrane tubular structure 400 in place, and providing adequate sealing against retrograde blood flow.

The distal end 401 of the membrane tubular structure 400 terminates with the valve flaps 403. The number of  
15 valve flaps 403 is directly proportional to the number of connecting members 105 supporting the membrane tubular assembly 102. The valve flaps 403 are sufficiently pliable and supple to easily open and close as the blood flow changes from antegrade to retrograde. When the valve flaps  
20 403 close (during retrograde flow) the interior surfaces of the flaps 403 and/or membrane tubular structure 400 come into contact to prevent or adequately reduce retrograde blood flow.

To facilitate closing the valve flaps 403 during retrograde blood flow, valve cusps 404 are formed into the membrane tubular structure 400. The valve cusps 404 are defined generally by the intersection of the connecting  
5 members 105 and membrane tubular structure 400.

The use of the term "cusps" is not meant to limit the scope of this invention. Although the term "cusps" is often more aptly used to describe the valve members in semilunar valves, such as the aortic and pulmonary valves, this  
10 discussion refers to both the cusps of semilunar valves and the "leaflets" of venous and atrioventricular valves. Accordingly, it should be understood that the aspects discussed in relation to these valves could be applied to any type of mammalian valve, including heart valves, venous  
15 valves, peripheral valves, etc.

During retrograde flow, blood passes the leading edge of valve flaps 403 and enters the valve cusps 404. Since the membrane tubular structure 400 (and membrane assembly 102) is substantially sealed against the inner vessel wall  
20 by proximal anchor 103, the valve cusps 404 form a substantially fluid tight chamber. As the valve cusps 404 fill, the membrane tubular structure 400 is directed inward until the interior surfaces of the membrane tubular

structure 400 contact each other, particularly along the leading edges of valve flaps 403, closing the membrane assembly 102. Figure 5A and 5B show perspective and section views, respectively, illustrating one embodiment of the expanded (deployed) prosthetic venous valve assembly 100 in the closed position.

In a preferred embodiment of the invention, the membrane assembly 102 is normally configured in the open position, and only moves to the closed position upon retrograde blood flow. This configuration minimizes interference with blood flow (minimized blocking) and reduces turbulence at and through the valve. The connecting members 105 in this embodiment have an inferior radial stiffness, and provide a natural bias against the movement of the membrane assembly 102 to the closed position. This bias assists the valve flaps 403 and valve cusps 404 when returning to the open position.

Depending on the application, it may also be desired that the bias towards opening the membrane assembly 102 (against closing) be sufficiently high to commence opening the valve before antegrade blood flow begins, i.e. during a point in time when the blood flow is stagnant (there is

neither antegrade nor retrograde blood flow), or when minimal retrograde flow is experienced.

In other applications, it may be desirable to have the valve assembly normally configured in the closed position, biased closed, and only open upon antegrade flow.

As earlier described, the membrane assembly 102 is made from a flexible membrane-like biocompatible material formed into the membrane tubular structure 400. The membrane 400 can be woven, non-woven (such as electrostatic spinning), mesh, knitted, film or porous film (such as foam).

The membrane assembly 102 may be fixedly attached to the structural frame by many different methods, including attachment resulting from radial pressure of the structural frame 101 against the membrane assembly 102, attachment by means of a binder, heat, or chemical bond, and/or attachment by mechanical means, such as welding or suturing. Preferably some of the membrane assembly 102, such as distal end 402 of tubular membrane 400, is slideably attached to the structural frame 101, particularly along connecting members 105. Allowing the distal end 402 to slide along the connecting members 105 may allow or improve the opening and closing of the flaps 403. The sliding movement may also assist the cusps 404 when filling and emptying.

In some applications, excessive sliding movement of the membrane assembly 102 is undesirable. In these embodiments, a limiting means may be integrated into the prosthetic valve 100 to limit the sliding movement of the membrane assembly 102. Examples of limiting means are shown in Figures 6A to 6C. In each embodiment a stop 600 (illustrated as stop 600A, 600B, and 600C in Figures 6A to 6C respectively) is integrated into the connecting member 105. The membrane assembly 102 is wrapped around the connecting member 105 and bonded to itself to form a loop collar 605. The loop collar 605 must be sized to inhibit the distal end 402 of the membrane assembly 102 from sliding past the stop 600. In Figure 6A, the connecting member 105 has a thickened or "bulbous" section forming stop 600A. Figure 6B illustrates an undulating stop 600B configuration. Similarly, Figure 6C shows the stop 600C configured as a double bulbous section. It should be noted that the various configurations illustrated in Figures 6A through 6C are exemplary. One of ordinary skill in the art would understand that other configurations of stops may be used.

In one embodiment of the invention the tubular membrane 400 is manufactured from a polymeric membrane, such as a micro-cellular foam or porous polymeric material. One

method for forming the membrane material over and around the structural frame 101 is shown in Figure 7. This method is presented in the context of a prosthetic valve application. However, the method may be applied generally to any application where a micro-cellular foam or porous polymeric material, particularly an ePTFE membrane, needs to be placed over and around a radially expandable and collapsible structural frame. Exemplary structural frames may include stents, stents grafts, valves (including percutaneously delivered venous valves), AAA (Abdominal Aortic Aneurysm) devices, local drug delivery devices, and the like. Accordingly, the disclosed medical device is not meant to limit the scope of the inventive method.

In this embodiment, a tubular structure fabricated from a polymeric material that can be processed such that it exhibits an expanded cellular structure, preferably expanded Polytetrafluoroethylene (ePTFE), is provided. The ePTFE tubing is made by expanding Polytetrafluoroethylene (PTFE) tubing, under controlled conditions, as is well known in the art. This process alters the physical properties that make it satisfactory for use in medical devices. An ePTFE tube having an Inter Nodal Distance (IND) in the range of approximately 20 $\mu$ m to approximately 200 $\mu$ m, and preferably

approximately 50 $\mu$ m to approximately 100 $\mu$ m has been found to be acceptable. However, one of ordinary skill in the art would understand that other materials that possess the necessary characteristics could also be used.

5       The method comprises first providing a polymeric tube, preferably an ePTFE tube, having a first inside diameter and a first wall thickness as shown in step 700. This polymeric tube, when fully radially expanded will have a second inside diameter and second wall thickness.

10       The inside diameter of the polymeric tube, before and after full radial expansion, is an important factor. To achieve proper seating and affixation of the membrane 400, the polymeric tube should be generally sized so that there is an interference fit between the inside diameter of the  
15       tube and outside diameter of the structural frame when fully expanded. The actual first inside diameter and first wall thickness of the tube are variable, and are typically determined by the type and application of the medical device being made. By way of example using venous valve  
20       applications, it has been found that a polymeric tube having a first inside diameter of approximately 1mm to 5mm and a wall thickness of approximately 25 $\mu$ m to 100 $\mu$ m, are acceptable. Preferably, the polymeric tube for venous valve



applications will have a first inside diameter of approximately 2mm to 3mm and a wall thickness of approximately 25 $\mu$ m to 50 $\mu$ m. This configuration should lead to a membrane 400 having a wall thickness of approximately 5 12 $\mu$ m to 50 $\mu$ m, and preferably in the range approximately 12 $\mu$ m to 25 $\mu$ m when the valve is deployed, i.e. full radial expansion.

A radially expandable and collapsible structural frame is then radially contracted, as shown in step 710, to a 10 diameter that is slightly smaller than the first inside diameter of the polymeric tube. In some embodiments, the radially expandable structural frame may be fabricated in the radially contracted pre-deployed state. In such instances, contraction of the radially expandable structural 15 frame may not be necessary.

Contraction of the structural frame may be achieved by several different methods. One particular method useful in embodiments where the structural frame is of the self-expanding type includes crimping the structural frame and 20 then inserting the crimped structural frame into a sheath that has an inside diameter that is smaller than the outside diameter of the structural frame. The sheath is further sized to allow the radially contracted structural frame and

sheath to be inserted into the polymeric tube. The interior surface of the sheath may inherently possess low friction characteristics to reduce the effort needed to insert the structural frame.

5       Crimping involves radially contracting the structural frame with a crimping tool, machine or similar device. Crimping devices for radially contracting radially contractible structural frame are well known in the art.

10       The radially contracted structural frame is then introduced into the polymeric tube as shown in step 720. In a preferred embodiment, the structural frame is introduced into the polymeric tube in such a fashion that at least a portion of the radially contracted frame is covered by the tube.

15       Some polymeric tubes, such as ePTFE tubes, tend to longitudinally shrink when radially expanded. When materials having these characteristics are used, it may be desirable to use tubes that are longer than necessary to accommodate this shrinkage. Alternatively, much longer  
20       tubes can be used, and any longitudinal excess trimmed after full radial expansion.

Once positioned at the desired location, the structural frame is then radially expanded into the polymeric tube to a

second diameter. The second diameter of the polymeric tube is greater than the first diameter, and enables a mechanical interference fit between the tube and structural frame as shown in step 730. The combination structural frame and  
5 polymeric membrane may be referred to as a covered frame assembly.

Radial expansion of the structural frame may be executed by many different means, including through the expansion of a mechanical assist device, such as by the  
10 radial expansion of an inflation balloon, cage assembly or mandrel placed inside the frame assembly. In instances where the structural frame is held compressed using a sheath, such as where the structural frame is of a self expanding type, radial expansion of the structural frame may  
15 be performed by sliding the sheath back off the structural frame, thereby allowing the self expanding structural frame to radially self expand.

In another, more preferred embodiment, that can be used where the self expanding structural is fabricated of a shape  
20 memory alloy, such as Nitinol, the radial contraction and expansion of the structural frame 101 can take advantage of the shape memory characteristics of the material when cooled and subsequently heated. Shape memory materials, such as

Nitinol, possess little or no recoil ability when cooled, but exhibit a high degree of memory, i.e. the ability to return to a configured shape, when heated. Cooling the Nitinol structural frame 101 before radial contraction  
5 allows the structural frame to remain in the contracted configuration until being heated. Accordingly, the Nitinol structural frame 101 can be cooled, contracted, and then introduced into the polymeric tube without the need for a sheath. Once in place, the structural frame can be heated  
10 to activate the Nitinol memory characteristics, causing the Nitinol structural frame 101 to self expand to the pre-contraction size and configuration, thus expanding the polymeric tube.

In such instances, radial contraction of the structural  
15 frame may be performed by crimping, using a crimping machine as is well known in the art.

The polymeric tube is inherently radially plastic, and has very little recoil properties. As the structural frame is radially expanded against the polymeric tube, the  
20 polymeric tube similarly radially expands. This radial expansion causes the tube wall to thin, providing a polymeric tube with a second wall thickness that is smaller than the first wall thickness.

It is important to note that the radially expandable structural frame and polymeric tube must be sized appropriately to allow the desired second wall thickness to be attained when the structural frame is at its expanded  
5 deployed state. For venous valve applications, it has been found that a second wall thickness of approximately 12 $\mu$ m to 50 $\mu$ m is acceptable. Preferably, the polymeric tube for venous valve applications will form a membrane having a second wall thickness of approximately 12 $\mu$ m to 25 $\mu$ m after  
10 expansion to the second diameter.

In embodiments where self-expanding structural frames  
101 are used, the structural frame 101 may not initially achieve the desired second diameter when allowed to self expand into the polymeric tube. Instead, the self expanding  
15 structural frame and polymeric tube may expand to an equilibrium point, having an intermediate inside diameter greater than the first inside diameter, but smaller than the desired second inside diameter. In such instances, the self-expanding structural frame/polymeric tube may have to  
20 additionally be mechanically expanded.

As described previously, mechanical expansion may be by several different mechanical assist devices, such as by the radial expansion of an inflation balloon, cage assembly or

mandrel placed inside the frame assembly. Since the polymeric tube offers very little radial elasticity, i.e. is inherently radially plastic, it will not tend to recoil back to the intermediate equilibrium point once fully expanded to  
5 the desired second inside diameter. Instead, the structural frame 101 will be allowed to achieve its natural self-expanded second diameter. Accordingly, the polymeric tube will achieve and maintain the desired second inner diameter.

The expanded polymeric tube may then be attached to the  
10 frame assembly as shown in step 740. Attachment of the polymeric tube to the structural frame can be accomplished by several different methods, including attachment resulting from radial pressure of the structural frame against the polymeric tube, attachment by means of a binder, heat, or  
15 chemical bond, and/or attachment by mechanical means, such as by welding, adhesives or suturing. Preferably, the expanded polymer tube is mechanically attached to the structural frame by a coating process.

As earlier disclosed, the polymeric tube is preferably  
20 a micro-cellular foam or porous polymeric material. When the cover frame assembly is coated with a coating solution, the coating solution at least partially fills the pores in the polymeric tube and at least partially encapsulates the

structural frame. As the coating solution dries and cures, the solution binds to the polymeric tube through the pores, mechanically attaching the membrane to the structural frame. In addition to attaching the expanded polymeric tube to the  
5 structural frame, the coating becomes an integral part of the polymeric tube, and together they form the membrane structure e.g. membrane 400.

The coating solution is preferably a highly elastic polymer, such as fluoroelastomer. These highly elastic  
10 polymers can be applied to the covered frame assembly by using various methods, including, for example, spin coating, spray coating, dip coating, chemical vapor deposition, plasma coating, co-extrusion coating and insert molding.

In still another preferred embodiment, the covered  
15 frame assembly is first dip coated in a polymer solution, and then spun about its longitudinal axis to more evenly distribute the coating. Still other methods for coating the fiber spun structural frame would be obvious to one of skill in the art.

20 As disclosed earlier, the coating process may act to partially encapsulate and attach at least a portion of the expanded polymeric tube (i.e. the membrane assembly 102) to the structural frame 101. It should be noted that in some

embodiments of the invention, some movement between the membrane assembly 102 and the structural frame 101 is desired. Accordingly, not all of the covered frame assembly may be coated.

5       The coating process may also remove some porosity from the membrane material. However, it may be desirable to maintain some porosity in particular embodiments to promote biological cell grown on and within the membrane tubular structure.

10       The coating solution preferably comprises a polymer put into solution with a solvent, such as methanol. In addition to methanol, most solvents can be used with expanded Polytetrafluoroethylene (ePTE). As the solvent evaporates, the polymer comes out of solution forming the coating layer.

15       Accordingly, for the process to work properly, the solvent used in the coating solution should not dissolve or alter the polymeric tube being coated. By way of example, a coating solution of vinylidene fluoride/hexafluoropropylene/tetrafluoroethylene

20       (VDF/HFP/TFE) in methanol (methanol being the solvent) has been found to be a suitable solution for coating a polymeric tube.



In a preferred embodiment of the invention, the polymer comprising the coating includes Daikin's Dai-El T630, a thermoplastic elastomer based on vinylidene fluoride/hexafluoropropylene/tetrafluoroethylene

5 (VDF/HFP/TFE) and blends thereof. Other preferred polymers include siliconized polyurethanes, including silicone-urethane copolymers, and blends thereof. Silicone-urethane copolymers can consist of segmented polyetherurethane with aromatic urea as hard segments and poly

10 (tetramethyleneoxide) [PTMO] as soft segments. Silicone (20 to 25%) is added by replacing PTMO with polydimethylsiloxane, and fluorine (0.5 to 2%) can be added by surface-modifying end groups. Again, one of ordinary skill in the art would understand that other materials

15 having suitable characteristics may be used for the coating, for example, other polymers and blends thereof.

Preferred siliconized polyurethanes include Polymer Technology Group's Pursil, Carbosil, Purspan and Purspan F.

The coating process should continue until the membrane

20 (coating and radially expanded polymeric tube) achieves a wall thickness of approximately 12 $\mu$ m to 100 $\mu$ m or more, preferably approximately between 25 $\mu$ m to 50 $\mu$ m.

Once the coating process is complete, some post processing of the membrane structure may take place to achieve particular desired characteristics or configurations, and improve the mechanical bonding to the structural frame 101. This post processing step is shown as optional step 750 in Figure 7.

By way of example, for valve applications, the post processing step 750 may be used to form or shape valve cusps, similar to cusps 404, or valve flaps, such as flaps 403, in the membrane structure. In addition, post processing may change the characteristics of the membrane structure by thickening or thinning the membrane in particular locations. Thickening the membrane may add rigidity and reinforcement to a particular area. Thinning the membrane may make the membrane more pliable. Still other post processing procedures may change the physical shape of the membrane structure, for example, by forming the loop collar 605 along the distal edge of membrane assembly 102. The loop collar 605 may, for example, assist in controlling the translational and circumferential movement of the membrane assembly 102 along the connecting members 105. The loop collars 605 may also reduce fatigue and tear stresses in the membrane.

Figures 8A and 8B show an example of the result of a post processing step that forms a loop collar 605 according to one embodiment of the present invention. To achieve this result, the membrane tubular structure 400 is wrapped around  
5 at least one element of structural frame 101 (connecting member 105) and bonded to itself at bond point 800.

It is important to note that the local delivery of drug/drug combinations may be utilized to treat a wide variety of conditions utilizing any number of medical  
10 devices, or to enhance the function and/or life of the device. Medical devices that may benefit from this treatment include, for example, the frame based unidirectional flow prosthetic implant disclosed in the present invention.

15 Accordingly, in addition to the embodiments described above, therapeutic or pharmaceutical agents may be added to any component of the device during fabrication, including, for example, the polymeric tube or coating solution, membrane assembly or structural frame to treat any number of  
20 conditions. In addition, therapeutic or pharmaceutical agents may be applied to the device, such as in the form of a drug or drug eluting layer, or surface treatment after the device has been formed. In a preferred embodiment, the therapeutic

and pharmaceutic agents may include any one or more of the following: antiproliferative/antimitotic agents including natural products such as vinca alkaloids (i.e. vinblastine, vincristine, and vinorelbine), paclitaxel, 5 epidipodophyllotoxins (i.e. etoposide, teniposide), antibiotics (dactinomycin (actinomycin D) daunorubicin, doxorubicin and idarubicin), anthracyclines, mitoxantrone, bleomycins, plicamycin (mithramycin) and mitomycin, enzymes (L-asparaginase which systemically metabolizes L-asparagine 10 and deprives cells which do not have the capacity to synthesize their own asparagine); antiplatelet agents such as G(GP) 11<sub>b</sub>/111<sub>a</sub> inhibitors and vitronectin receptor antagonists; antiproliferative/antimitotic alkylating agents such as nitrogen mustards (mechlorethamine, 15 cyclophosphamide and analogs, melphalan, chlorambucil), ethylenimines and methylmelamines (hexamethylmelamine and thiotepa), alkyl sulfonates-busulfan, nirtosoureas (carmustine (BCNU) and analogs, streptozocin), trazenes - dacarbazine (DTIC); antiproliferative/antimitotic 20 antimetabolites such as folic acid analogs (methotrexate), pyrimidine analogs (fluorouracil, floxuridine, and cytarabine), purine analogs and related inhibitors (mercaptopurine, thioguanine, pentostatin and 2-

chlorodeoxyadenosine {cladribine}); platinum coordination complexes (cisplatin, carboplatin), procarbazine, hydroxyurea, mitotane, aminoglutethimide; hormones (i.e. estrogen); anticoagulants (heparin, synthetic heparin salts and other inhibitors of thrombin); fibrinolytic agents (such as tissue plasminogen activator, streptokinase and urokinase), aspirin, dipyridamole, ticlopidine, clopidogrel, abciximab; antimigratory; antisecretory (breveldin); anti-inflammatory: such as adrenocortical steroids (cortisol, cortisone, fludrocortisone, prednisone, prednisolone, 6 $\alpha$ -methylprednisolone, triamcinolone, betamethasone, and dexamethasone), non-steroidal agents (salicylic acid derivatives i.e. aspirin; para-aminophenol derivatives i.e. acetaminophen; indole and indene acetic acids (indomethacin, sulindac, and etodolac), heteroaryl acetic acids (tolmetin, diclofenac, and ketorolac), arylpropionic acids (ibuprofen and derivatives), anthranilic acids (mefenamic acid, and meclofenamic acid), enolic acids (piroxicam, tenoxicam, phenylbutazone, and oxyphenthatrazone), nabumetone, gold compounds (auranofin, aurothioglucose, gold sodium thiomalate); immunosuppressives: (cyclosporine, tacrolimus (FK-506), sirolimus (rapamycin), azathioprine, mycophenolate mofetil); angiogenic agents: vascular endothelial growth

factor (VEGF), fibroblast growth factor (FGF); angiotensin  
receptor blockers; nitric oxide donors; anti-sense  
oligonucleotides and combinations thereof; cell cycle  
inhibitors, mTOR inhibitors, and growth factor receptor  
5 signal transduction kinase inhibitors; retinoids; cyclin/CDK  
inhibitors; HMG co-enzyme reductase inhibitors (statins);  
and protease inhibitors.

While a number of variations of the invention have been  
shown and described in detail, other modifications and  
10 methods of use contemplated within the scope of this  
invention will be readily apparent to those of skill in the  
art based upon this disclosure. It is contemplated that  
various combinations or sub combinations of the specific  
embodiments may be made and still fall within the scope of  
15 the invention. For example, the embodiments variously shown  
to be prosthetic "venous valves" may be modified to instead  
incorporate prosthetic "heart valves" and are also  
contemplated. Moreover, all assemblies described are  
believed useful when modified to treat other vessels or  
20 lumens in the body, in particular other regions of the body  
where fluid flow in a body vessel or lumen needs to be  
controlled or regulated. This may include, for example, the  
coronary, vascular, non-vascular and peripheral vessels and

ducts. Accordingly, it should be understood that various applications, modifications and substitutions may be made of equivalents without departing from the spirit of the invention or the scope of the following claims.

- 5 The following claims are provided to illustrate examples of some beneficial aspects of the subject matter disclosed herein which are within the scope of the present invention.

**CLAIMS****WHAT IS CLAIMED IS:**

1. A method of making a medical device having a thin wall tubular structure over a radially contractible and expandable structural frame, the method comprising the steps of:
- providing a polymeric tube having a first diameter and a first wall thickness;
  - radially contracting the structural frame;
  - 10 placing the radially contracted structural frame at least partially into the polymeric tube;
  - expanding the structural frame to expand at least a portion of the polymeric tube to a second diameter having a second wall thickness, the second diameter of the polymeric
  - 15 tube being greater than the first diameter, the second wall thickness being smaller than the first wall thickness; and
  - mechanically attaching the expanded polymeric tube to the expanded structural frame.
- 20 2. The method of claim 1 wherein the step of radially contracting the structural frame comprises inserting the structural frame into a sheath, the sheath being sized to



have an inside diameter that is smaller than the outside diameter of the structural frame.

3. The method of claim 1 wherein the step of radially contracting the structural frame comprises:

- 5        radially crimping the structural frame with a crimping device to a reduced diameter; and
- cooling the radially crimped structural frame to temporarily maintain the radially contracted configuration.

10

4. The method of claim 1 wherein the step of radially expanding the structural frame comprises:

- inserting a radial expansion device into the structural frame along the structural frame's longitudinal axis;
- 15        radially expanding the radial expansion device to expand the structural frame.

5. The method of claim 4 wherein the radial expansion device is an inflation balloon.

20

6. The method of claim 4 wherein the radial expansion device is a radially expanding cage assembly.

7. The method of claim 4 wherein the radial expansion device is a radially expanding mandrel.

8. The method of claim 4 wherein the radial expansion device  
5 is a tapered mandrel.

9. The method of claim 1 wherein the step of radially expanding the structural frame comprises removing a sheath constraining the radially contracted structural frame,  
10 thereby allowing the structural frame to radially expand.

10. The method of claim 1 wherein the step of radially expanding the structural frame comprises heating the radially contracted structural frame.

15

11. The medical device of claim 1 wherein the step of mechanically attaching the expanded polymeric tube to the expanded structural frame, comprises suturing the polymeric tube to the structural frame.

20

12. The medical device of claim 1 wherein the step of mechanically attaching the expanded polymeric tube to the

expanded structural frame comprises welding the polymeric tube to the structural frame.

13. The medical device of claim 1 wherein the step of  
5 mechanically attaching the expanded polymeric tube to the expanded structural frame comprises adhering the polymeric tube to the structural frame with an adhesive.

14. The medical device of claim 1 wherein the step of  
10 mechanically attaching the expanded polymeric tube to the expanded structural frame comprises coating at least a portion of the expanded polymeric tube and the structural frame with a polymer.

15 15. The method of claim 14 wherein the step of coating comprises spraying a polymer solution over at least a portion of the expanded polymeric tube and structural frame.

16. The method of claim 14 wherein the step of coating  
20 comprises dipping at least a portion of the expanded polymeric tube and structural frame in a polymer solution.

17. The method of claim 14 wherein the step of coating comprises:

dipping at least a portion of the expanded polymeric tube and structural frame in a polymer solution; and

5 spinning the dip coated expanded polymeric tube and structural frame to evenly distribute the coating.

18. A method of placing a tubular structure about a radially contractible and expandable structural frame, the  
10 method comprising the steps of:

providing a porous polymeric tube having a first diameter and a first wall thickness;

radially contracting the structural frame;

placing the radially contracted structural frame at  
15 least partially into the porous polymeric tube;

expanding the structural frame to expand at least a part of the porous polymeric tube to a second diameter, the second diameter of the porous polymeric tube being greater than the first diameter; and

20 coating at least a portion of the expanded porous polymeric tube and the expanded structural frame, thereby mechanically attaching the expanded porous polymeric tube to the expanded structural frame.

19. The method of claim 18 wherein the step of mechanically attaching the expanded porous polymeric tube to the expanded structural frame comprises:

- 5       filling the at least a portion of the pores in the coated porous polymeric tube with a polymer solution; and  
          curing the polymer solution, thereby mechanically bonding the porous polymeric tube to the coated structural frame.

10

20. The method of claim 1 further comprising performing post processing of the expanded polymeric tube.

21. The method of claim 20 wherein the step of post  
15       processing includes reshaping the expanded polymeric tube.

22. The method of claim 20 wherein the step of post processing includes thinning at least a portion of the expanded polymeric tube.

20

23. The method of claim 20 wherein the step of post processing includes thickening at least a portion of the expanded polymeric tube.

24. The method of claim 20 wherein the step of post processing includes forming cusps in the expanded polymeric tube.

5

25. A medical device having a tubular membrane structure comprising:

a radially expandable and collapsible structural frame;

a thin wall membrane positioned over the radially  
10 expandable and collapsible structural frame, the membrane formed at least in part by radially expanding a polymeric tube with the structural frame; and

a coating over the thin wall membrane, the coating and thin wall membrane forming the tubular membrane structure,  
15 and wherein the coating mechanically attaches the thin wall membrane to the structural frame.

26. The medical device of claim 25 wherein the structural frame comprises a lattice of interconnected  
20 elements, and having a substantially cylindrical configurations with first and second open ends and a longitudinal axis extending there between.

27. The medical device of claim 25 wherein the thin wall membrane comprises ePTFE.

28. The medical device of claim 25 wherein the  
5 polymeric tube has a wall thickness before radial expansion in the range from about 25 $\mu$ m to about 50 $\mu$ m.

29. The medical device of claim 25 wherein the thin wall membrane has a wall thickness after radial expansion in  
10 the range from about 12 $\mu$ m to about 25 $\mu$ m

30. The medical device of claim 25 wherein the coating comprises a polymer.

15 31. The medical device of claim 30 wherein the polymer coating comprises an elastomeric polymer.

32. The medical device of claim 31 wherein the elastomeric polymer comprises an elastomeric fluoropolymer.

20

33. The medical device of claim 32 wherein the elastomeric fluoropolymer comprises a vinylidene fluoride/hexafluoropropylene/tetrafluoroethylene.

34. The medical device of claim 31 wherein the elastomeric polymer comprises siliconized polyurethane.

5 35. The medical device of claim 34 wherein the siliconized polyurethane comprises segmented polyetherurethane.

36. The medical device of claim 25 wherein the coating  
10 has a wall thickness from about 12 $\mu$ m to about 25 $\mu$ m.

37. The medical device of claim 25 wherein the thin wall membrane comprises a therapeutic agent.

15 38. The medical device of claim 25 wherein the thin wall membrane comprises a pharmaceutical agent.

39. The medical device of claim 25 wherein the coating comprises a therapeutic agent.

20

40. The medical device of claim 25 wherein the coating comprises a pharmaceutical agent.



41. The medical device of claim 25 wherein at least a portion of the structural frame is coated with a therapeutic agent.

5 42. The medical device of claim 25 wherein at least a portion of the structural frame is coated with a pharmaceutical agent.

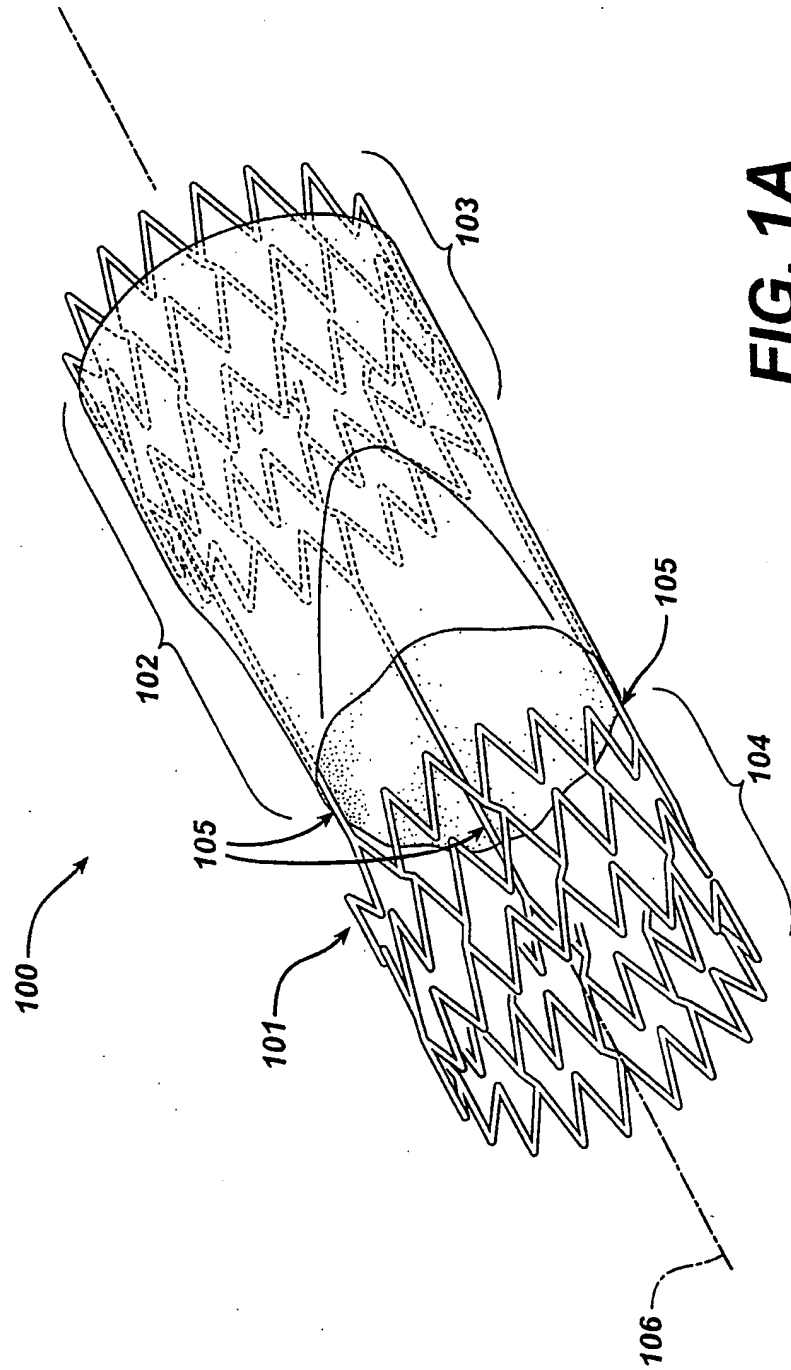


FIG. 1A

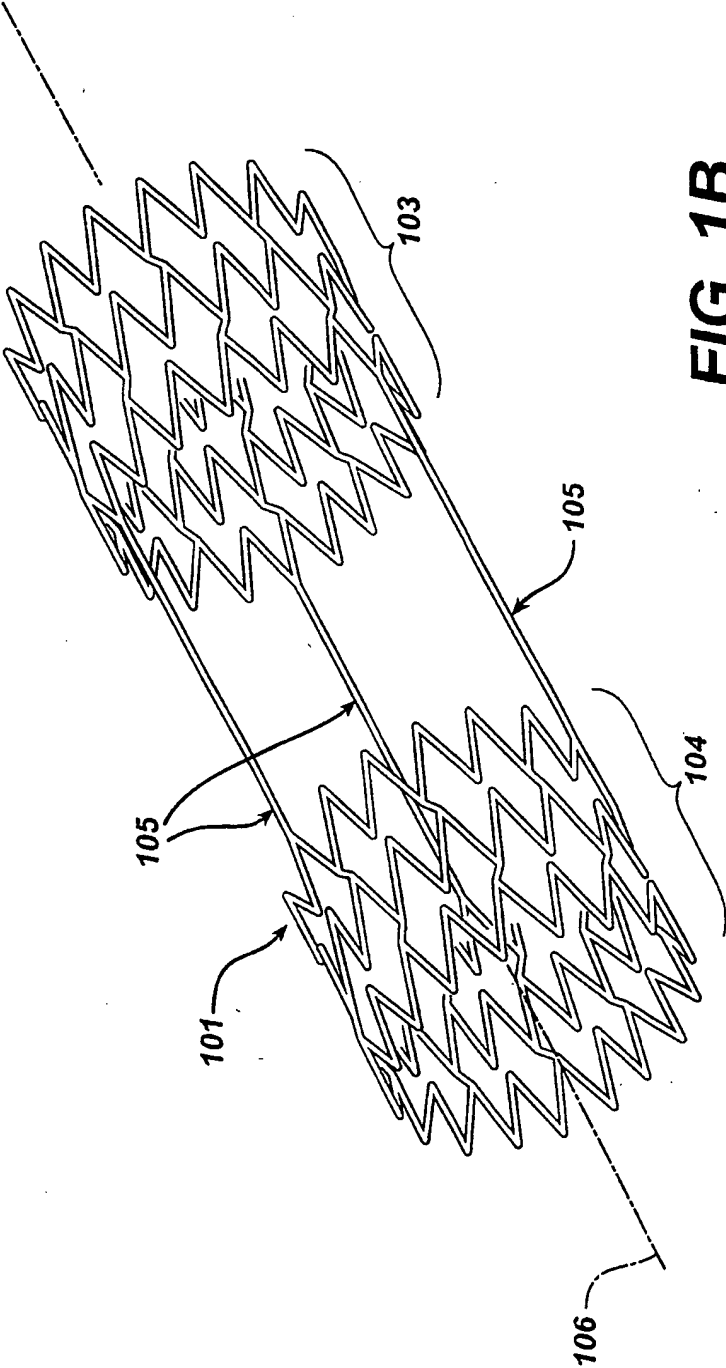


FIG. 1B

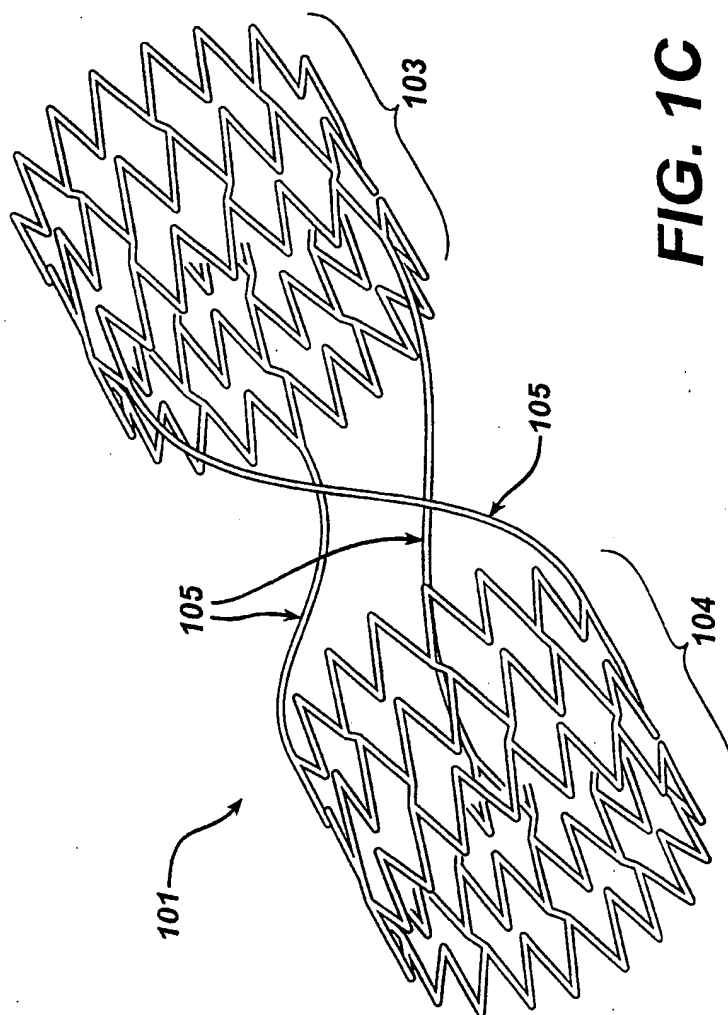


FIG. 1C

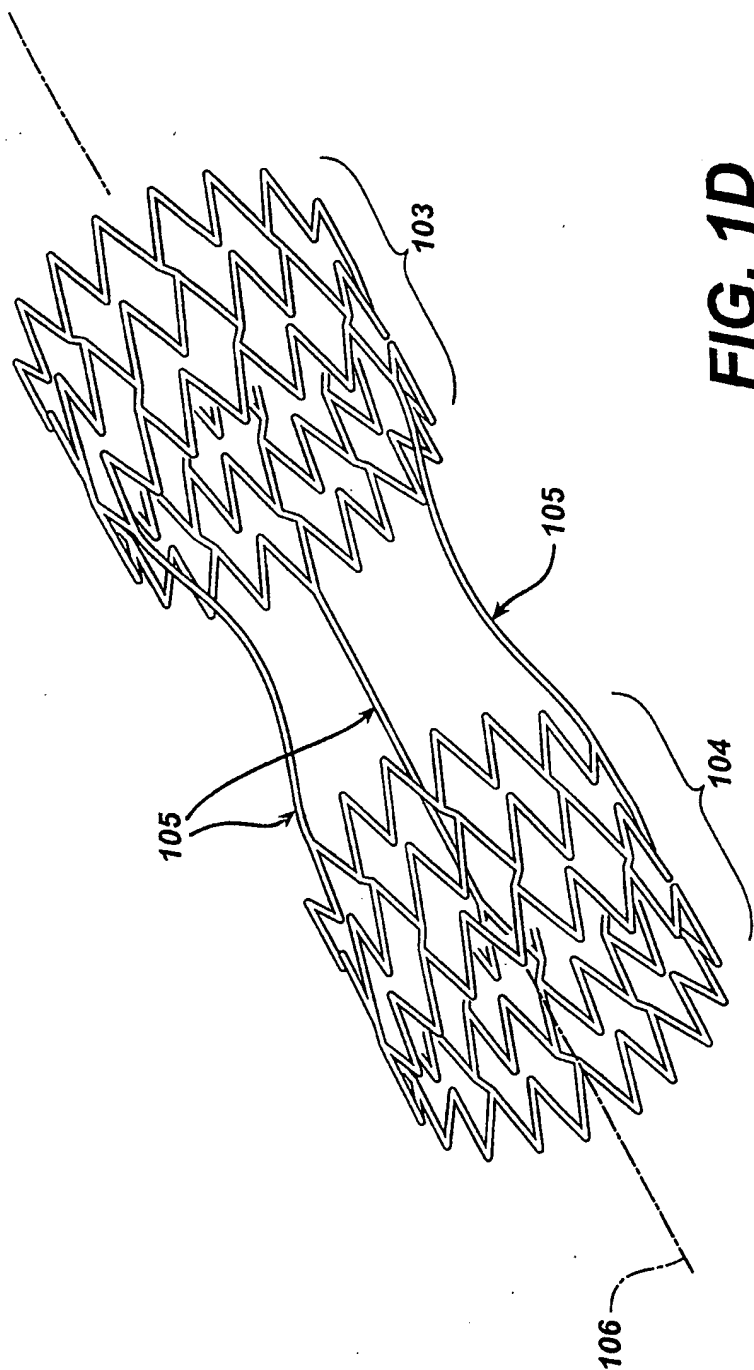
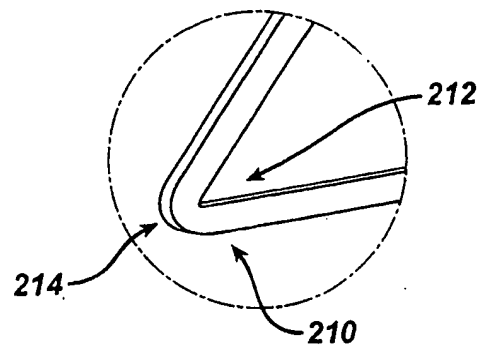
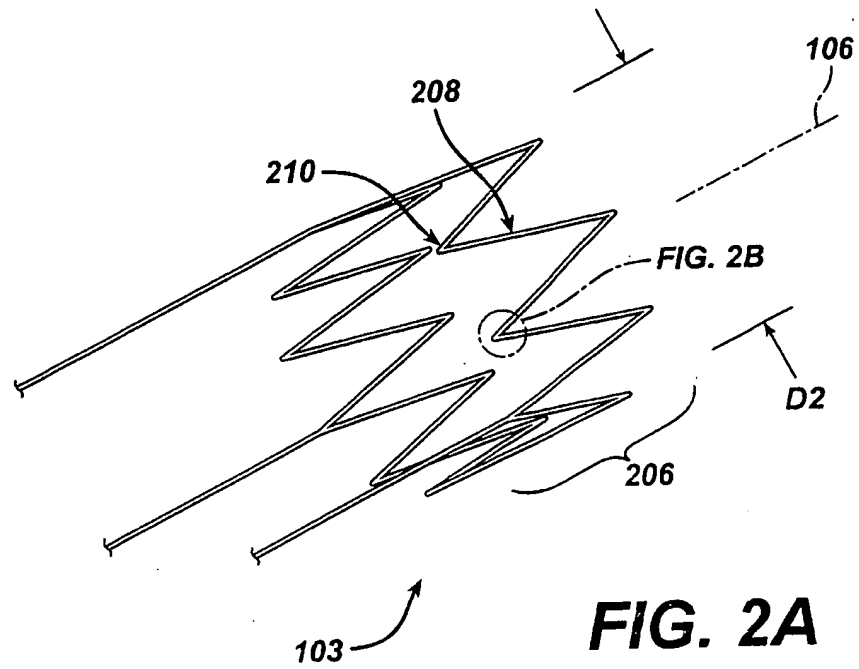


FIG. 1D



**FIG. 2B**

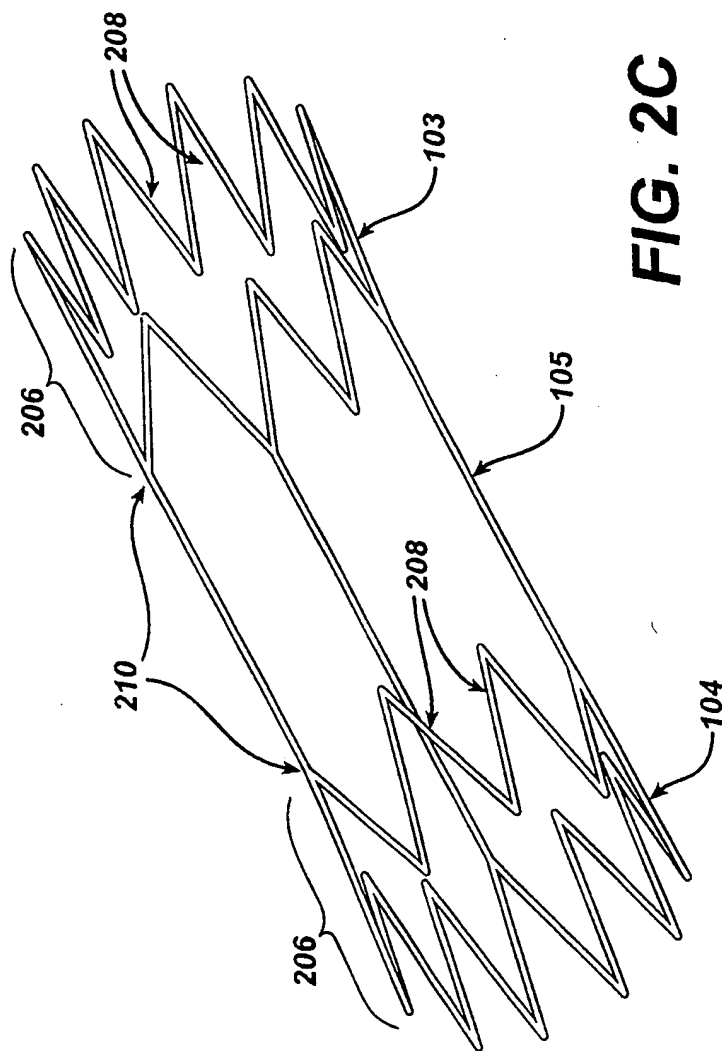
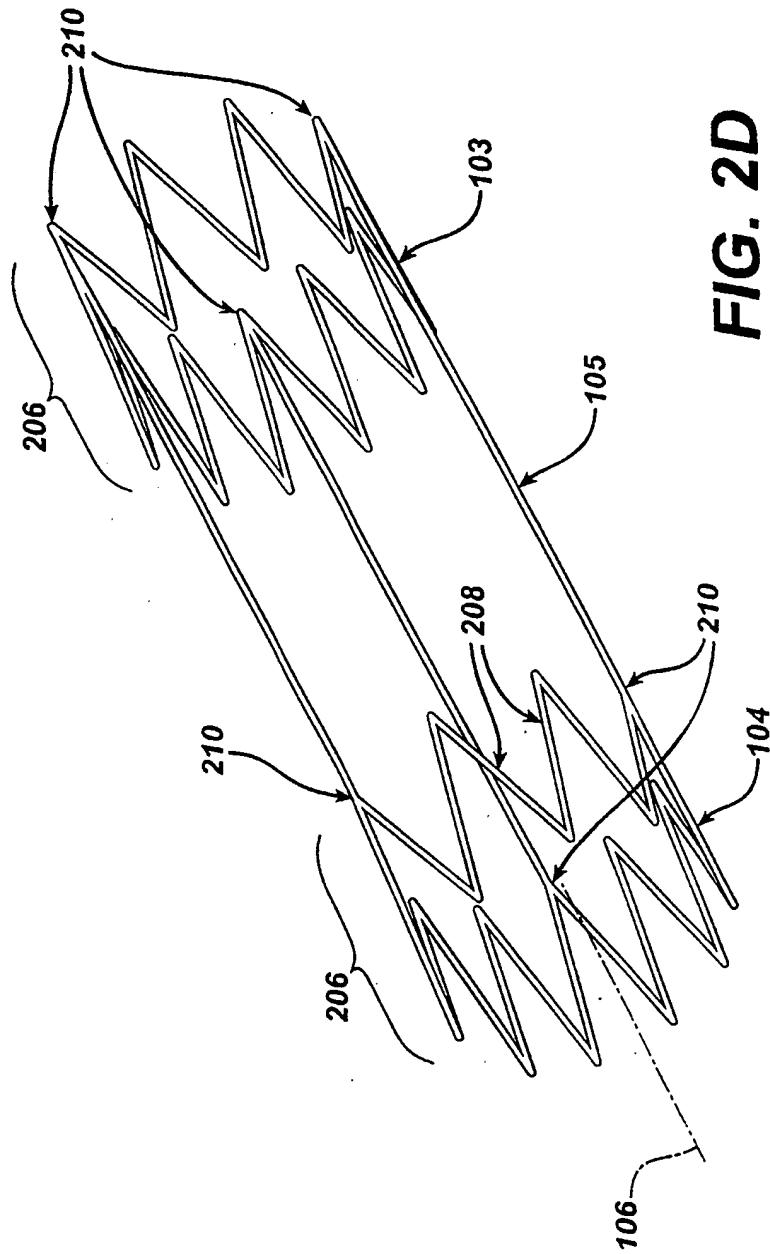


FIG. 2C



**FIG. 2D**



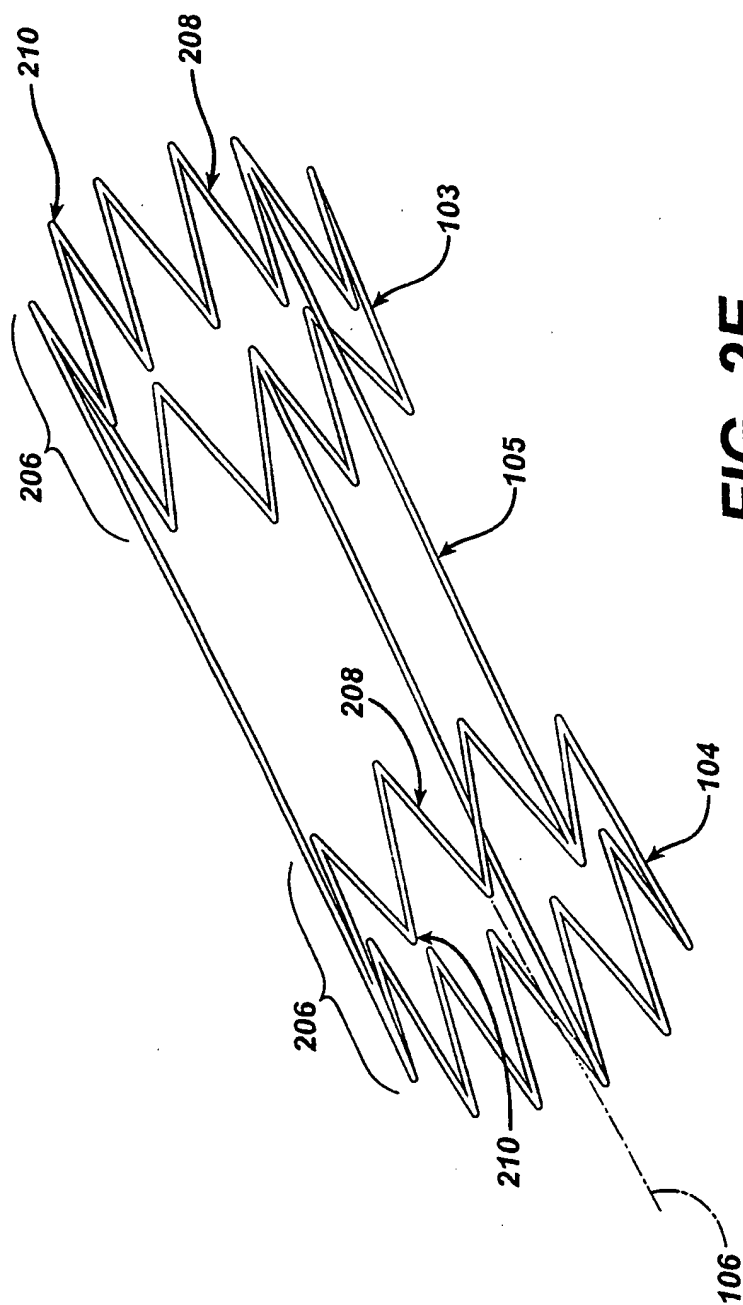


FIG. 2E

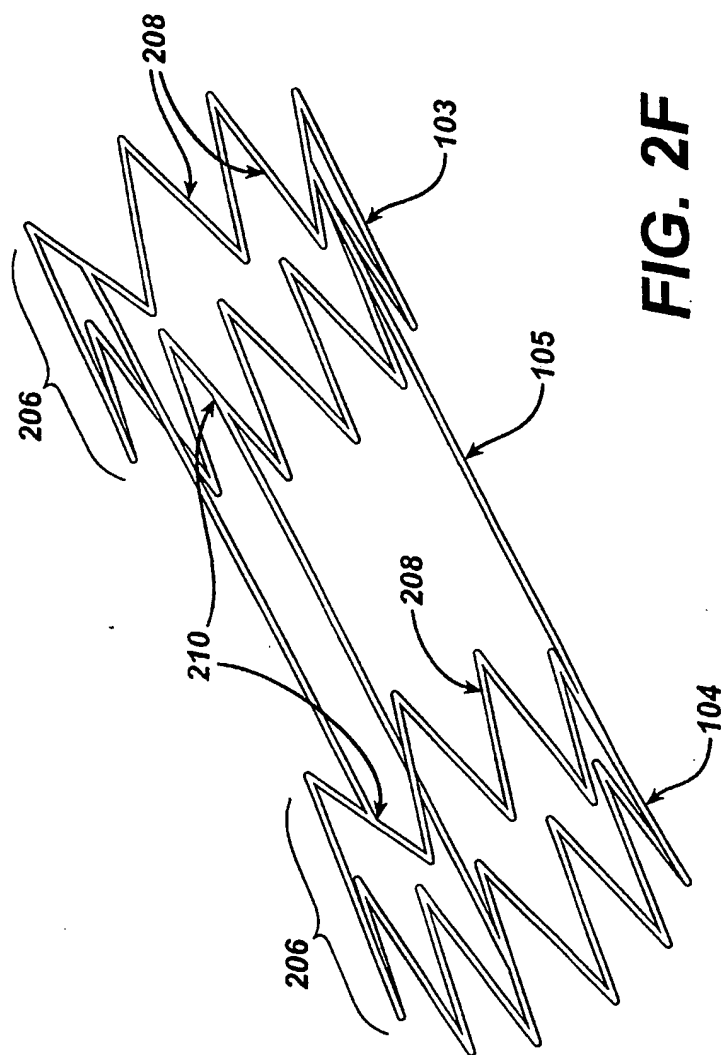


FIG. 2F

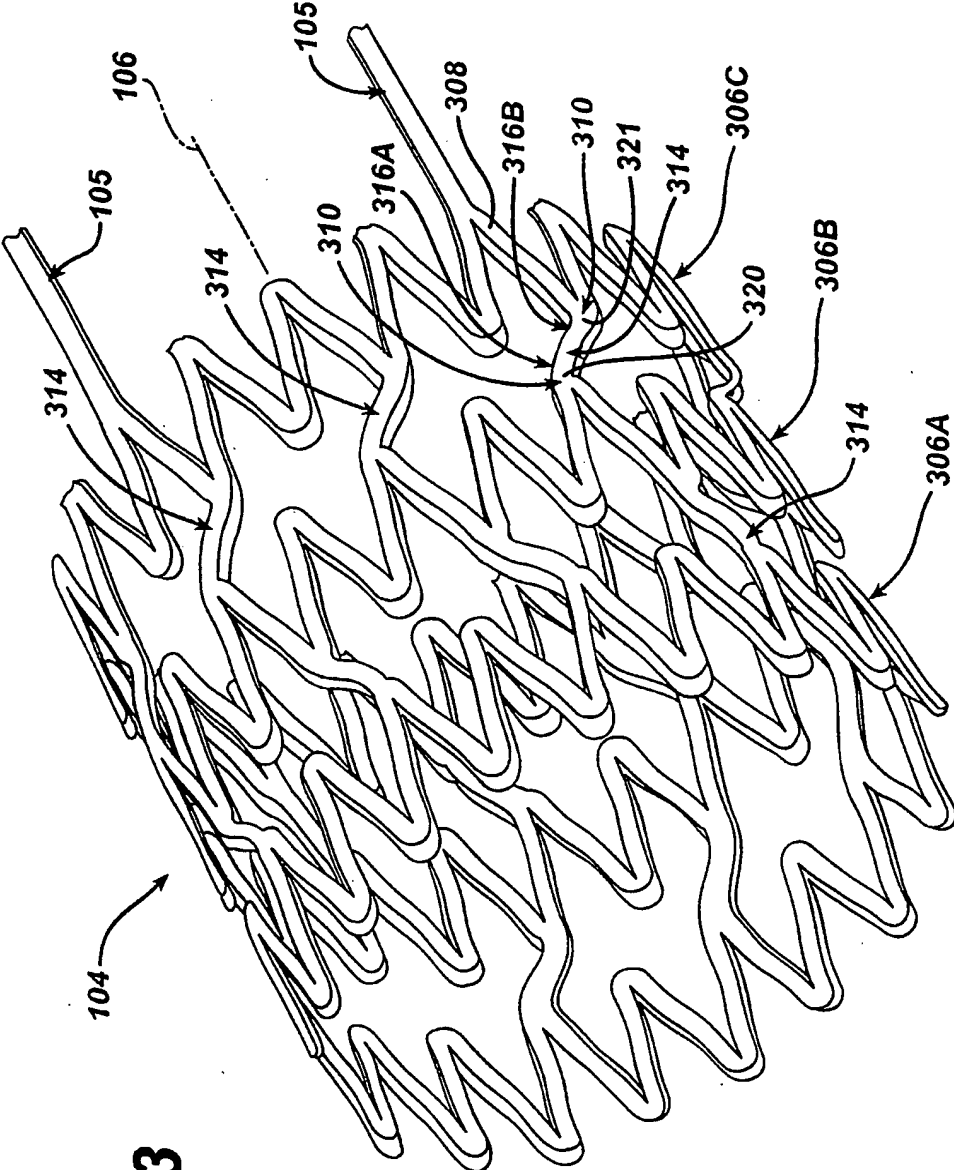
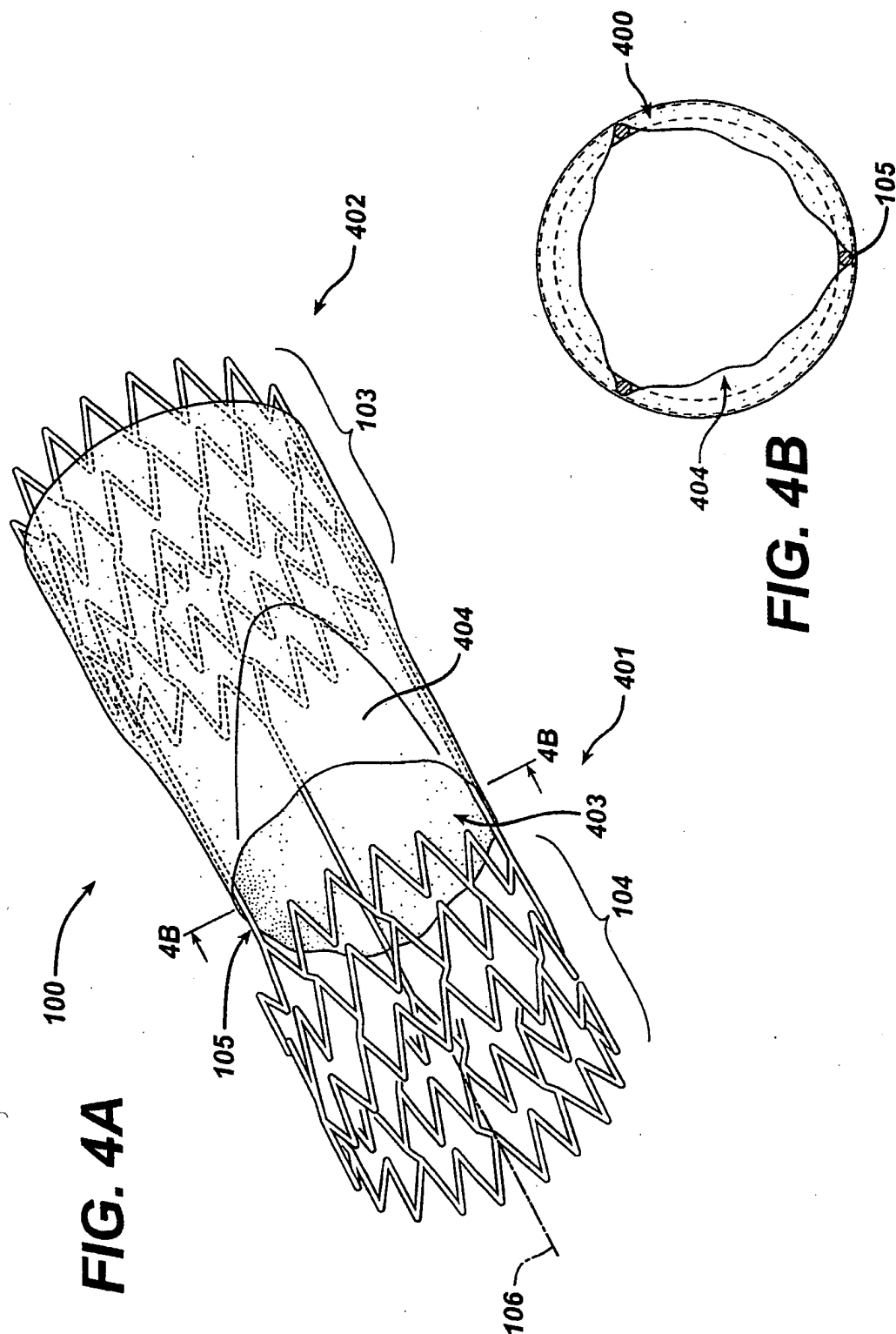
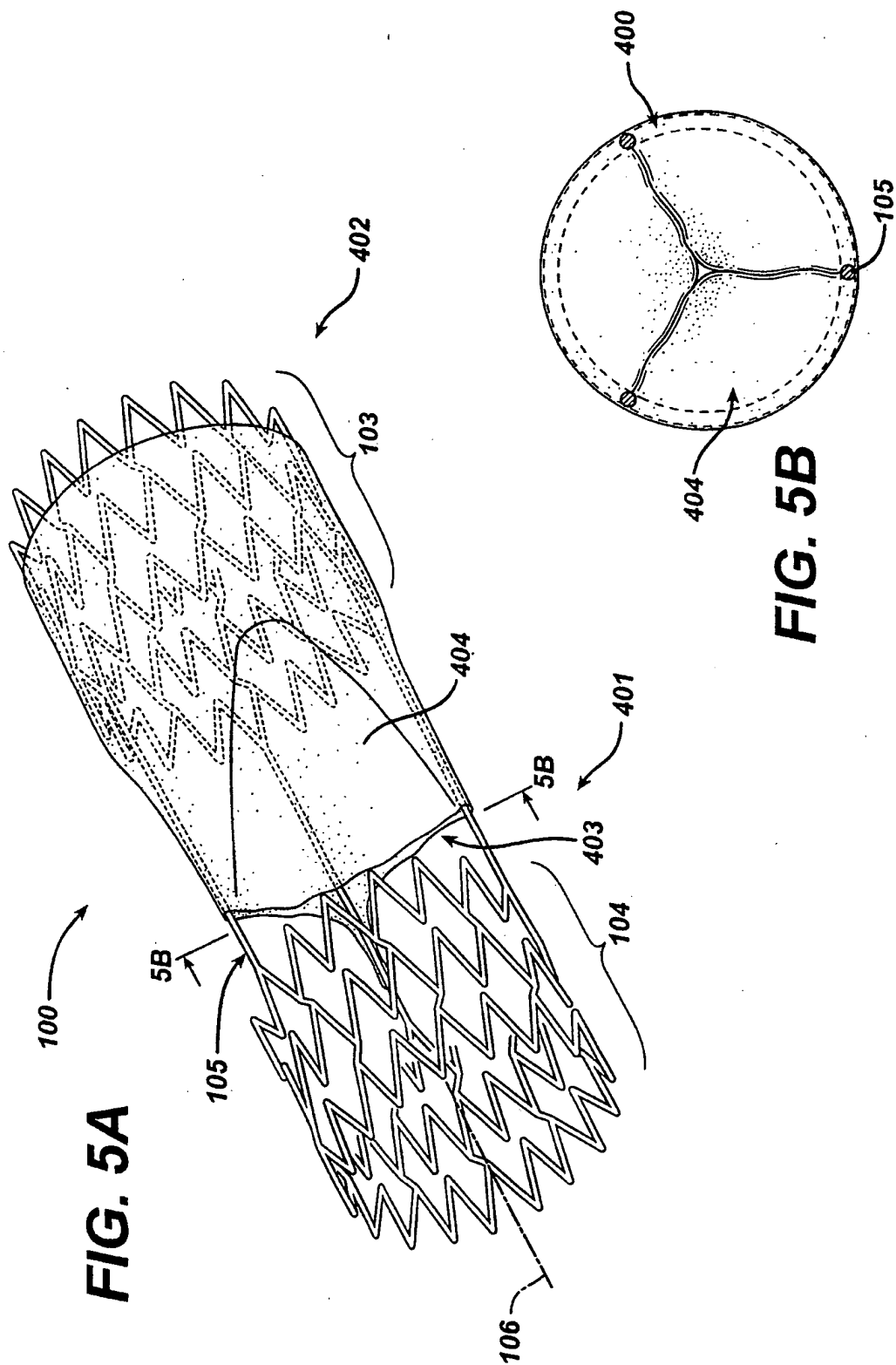
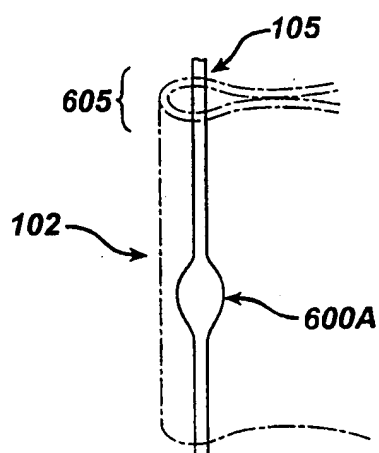
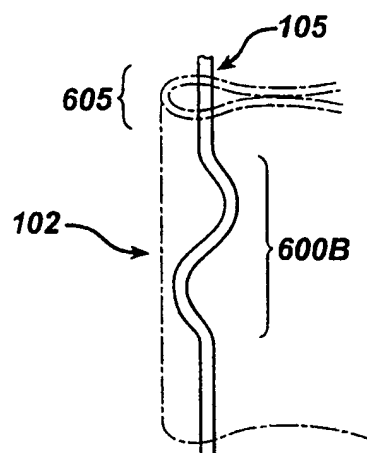
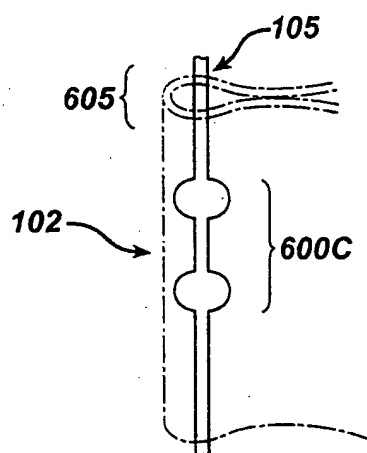
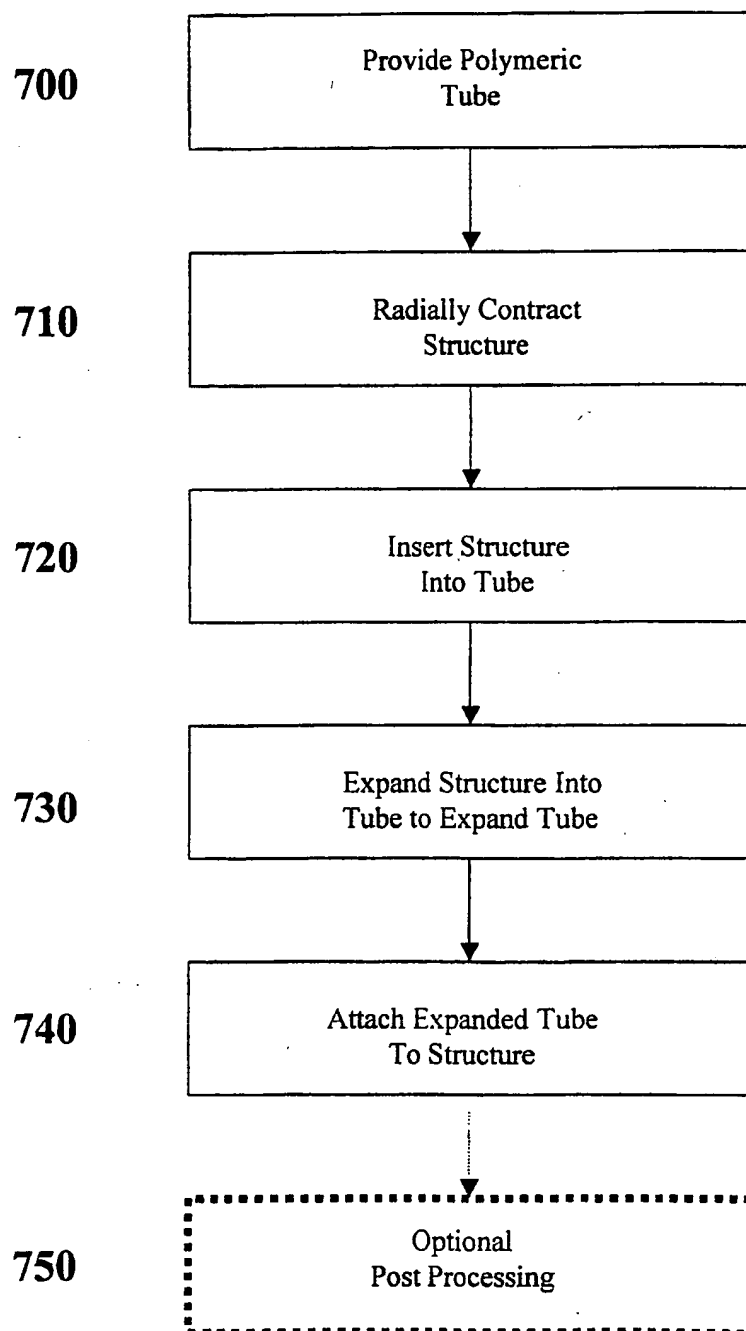


FIG. 3





**FIG. 6A****FIG. 6B****FIG. 6C**

**Figure 7**

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 03/14009

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61F2/06

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	EP 0 938 879 A (MEDTRONIC AVE INC) 1 September 1999 (1999-09-01)  paragraph '0085! - paragraph '0088! paragraph '0077!	25-31, 39-42 32-35, 37, 38
Y	EP 1 192 957 A (ETHICON INC) 3 April 2002 (2002-04-03) claims 1-9	32, 33, 37, 38
Y	US 5 607 463 A (SCHWARTZ ROBERT S ET AL) 4 March 1997 (1997-03-04) column 10, line 3 - line 13  -/-	34, 35

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

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Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

International Application No  
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 6 375 787 B1 (LUKIC GORAN) 23 April 2002 (2002-04-23)  column 2, line 36 -column 3, line 7 figures 1,2	25, 26, 30, 31 1, 18
A	WO 01 67992 A (YANG JUN) 20 September 2001 (2001-09-20) & US 2002/143385 A1 (YANG JUN) 3 October 2002 (2002-10-03) paragraph '0041! paragraph '0042!	1, 18
A	US 6 245 100 B1 (DAVILA LUIS A ET AL) 12 June 2001 (2001-06-12) column 4, line 9 - line 15 figure 8	1, 18

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/14009

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0938879	A	01-09-1999	US 6488701 B1	03-12-2002
			DE 938879 T1	20-04-2000
			EP 0938879 A2	01-09-1999
			ES 2141071 T1	16-03-2000
			US 2003028240 A1	06-02-2003
EP 1192957	A	03-04-2002	AU 1129902 A	08-04-2002
			AU 1132102 A	08-04-2002
			AU 7730201 A	11-04-2002
			AU 9316101 A	08-04-2002
			AU 9486901 A	08-04-2002
			CA 2357881 A1	29-03-2002
			CA 2424029 A1	04-04-2002
			CA 2424038 A1	04-04-2002
			CA 2424049 A1	04-04-2002
			CA 2425753 A1	04-04-2002
			EP 1192957 A2	03-04-2002
			EP 1335761 A1	20-08-2003
			EP 1322235 A1	02-07-2003
			EP 1322351 A1	02-07-2003
			EP 1322342 A1	02-07-2003
			JP 2002238994 A	27-08-2002
			WO 0226280 A1	04-04-2002
			WO 0226139 A1	04-04-2002
			WO 0226281 A1	04-04-2002
			WO 0226271 A1	04-04-2002
			US 2002094440 A1	18-07-2002
			US 2002111590 A1	15-08-2002
			US 2002133183 A1	19-09-2002
			US 2002051730 A1	02-05-2002
US 5607463	A	04-03-1997	NONE	
US 6375787	B1	23-04-2002	EP 0621015 A1	26-10-1994
			US 5534287 A	09-07-1996
			US 2002096252 A1	25-07-2002
			AT 164056 T	15-04-1998
			CA 2114891 A1	24-10-1994
			CA 2205533 A1	24-10-1994
			CA 2206709 A1	24-10-1994
			CA 2206712 A1	24-10-1994
			CA 2255476 A1	24-10-1994
			DE 69317548 D1	23-04-1998
			DE 69317548 T2	13-08-1998
			DK 621015 T3	21-12-1998
			ES 2114964 T3	16-06-1998
			JP 2914420 B2	28-06-1999
			JP 7000529 A	06-01-1995
WO 0167992	A	20-09-2001	US 2002143385 A1	03-10-2002
			AU 4736001 A	24-09-2001
			WO 0167992 A1	20-09-2001
			US 2003009213 A1	09-01-2003
US 6245100	B1	12-06-2001	AU 1669601 A	02-08-2001
			CA 2333339 A1	01-08-2001
			JP 2001245990 A	11-09-2001

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